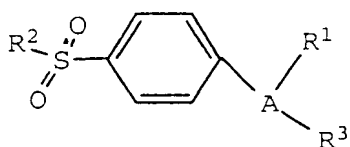


What is claimed is :

1. A combination comprising a therapeutically-effective amount of a cyclooxygenase-2 inhibitor, a leukotriene B₄ receptor antagonist and an immunosuppressive drug, wherein the immunosuppressive drug is selected from the group consisting of antiproliferative agents, antiinflammatory-acting compounds and inhibitors of leukocyte activation.

2. The combination of Claim 1 wherein the cyclooxygenase-2 inhibitor is selected from Dupont Dup-697, Taisho NS-398, meloxicam, flosulide or compounds of Formula I



I

wherein:

A is a 5- or 6-member ring substituent selected from partially unsaturated or unsaturated heterocyclo or carbocyclic rings;

R^1 is at least one substituent selected from the group consisting of heterocyclo, cycloalkyl, cycloalkenyl and aryl, wherein R^1 is optionally substituted at a substitutable position with one or more radicals selected from the group consisting of alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

R^2 is selected from the group consisting of alkyl, and amino; and

R^3 is a radical selected from the group consisting of halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocyclooxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclo,

cycloalkenyl, aralkyl, heterocycloalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, 5 aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-10 alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-arylaminominoalkyl, N-aralkylaminominoalkyl, N-alkyl-N-aralkylaminominoalkyl, N-alkyl-N-arylaminominoalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-15 arylaminosulfonyl, arylsulfonyl, and N-alkyl-N-arylaminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

3. The combination of Claim 1 wherein the 20 leukotriene B₄ receptor antagonist is selected from the group consisting of calcitriol, ontazolast, Bayer Bay-x-1005, Ciba-Geigy CGS-25019C, ebselen, Leo Denmark ETH-615, Lilly LY-293111, Ono ONO-4057, Terumo TMK-688, Boehringer Ingleheim BI-RM-270, Lilly LY 213024, Lilly 25 LY 264086, Lilly LY 292728, Ono ONO LB457, Pfizer 105696, Perdue Frederick PF 10042, Rhone-Poulenc Rorer RP 66153, SmithKline Beecham SB-201146, SmithKline Beecham SB-201993, SmithKline Beecham SB-209247, Searle SC-53228, Shionogi S-2472, Searle SC-52798, Leo Denmark 30 SR-2566, Tanabe T-757, Sumitamo SM 15178, and American Home Products WAY 121006.

4. The combination of Claim 3 wherein the 35 leukotriene B₄ receptor antagonist is selected from the group consisting of calcitriol, ontazolast, Bayer Bay-x-1005, Ciba-Geigy CGS-25019C, ebselen, Leo Denmark ETH-615, Lilly LY-293111, Ono ONO-4057, SmithKline Beecham SB-201993, SmithKline Beecham SB-209247, Warner-Lambert

BPC-15, Pfizer 105696, Shionogi S-2472, Searle SC-52798, Leo Denmark SR-2566, Tanabe T-757, and Terumo TMK-688.

5 5. The combination of Claim 2 wherein the cyclooxygenase-2 inhibitor is selected from compounds of Formula I.

10 6. The combination of Claim 5 wherein A is selected from the group consisting of oxazolyl, isoxazolyl, thienyl, dihydrofuryl, furyl, pyrrolyl, pyrazolyl, thiazolyl, imidazolyl, isothiazolyl, cyclopentenyl, phenyl, and pyridyl; wherein R^1 is selected from the group consisting of 5- and 6-membered heterocyclo, lower cycloalkyl, lower cycloalkenyl and aryl, wherein the
15 aryl is selected from the group consisting of phenyl, biphenyl and naphthyl, wherein R^1 is optionally substituted at a substitutable position with one or more radicals selected from the group consisting of lower alkyl, lower haloalkyl, cyano, carboxyl, lower
20 alkoxycarbonyl, hydroxyl, lower hydroxyalkyl, lower haloalkoxy, amino, lower alkylamino, phenylamino, nitro, lower alkoxyalkyl, lower alkylsulfinyl, halo, lower alkoxy and lower alkylthio; wherein R^2 is selected from the group consisting of lower alkyl and amino; and
25 wherein R^3 is a radical selected from the group consisting of halo, lower alkyl, oxo, cyano, carboxyl, lower cyanoalkyl, heteroaryloxy, lower alkyloxy, lower cycloalkyl, phenyl, lower haloalkyl, 5- or 6-membered heterocyclo, lower hydroxylalkyl, lower aralkyl, acyl,
30 phenylcarbonyl, lower alkoxyalkyl, heteroaryloxy, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, alkylamino, aminoalkyl, alkylaminoalkyl, aryloxy, and aralkoxy; or a pharmaceutically-acceptable salt thereof.

35 7. The combination of Claim 6 wherein A is selected from the group consisting of oxazolyl, isoxazolyl, dihydrofuryl, imidazolyl, and pyrazolyl; wherein R^1 is selected from the group consisting of 5-

and 6-membered heterocyclo, and aryl, wherein aryl is selected from the group consisting of phenyl, biphenyl and naphthyl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals
5 selected from the group consisting of lower alkyl, lower haloalkyl, cyano, carboxyl, lower alkoxycarbonyl, hydroxyl, lower hydroxyalkyl, lower haloalkoxy, amino, lower alkylamino, phenylamino, nitro, lower alkoxyalkyl, lower alkylsulfinyl, halo, lower alkoxy and lower
10 alkylthio; wherein R² is amino; and wherein R³ is a radical selected from the group consisting of oxo, cyano, carboxyl, lower alkoxycarbonyl, lower carboxyalkyl, lower cyanoalkyl, halo, lower alkyl, lower alkyloxy, lower cycloalkyl, phenyl, lower haloalkyl, 5-
15 or 6-membered heterocyclo, lower hydroxylalkyl, lower aralkyl, acyl, phenylcarbonyl, lower alkoxyalkyl, 5- or 6-membered heteroaryloxy, aminocarbonyl, lower alkylaminocarbonyl, lower alkylamino, lower aminoalkyl, lower alkylaminoalkyl, phenyloxy, and lower aralkoxy; or
20 a pharmaceutically-acceptable salt thereof.

8. The combination of Claim 7 wherein A is selected from the group consisting of oxazolyl, isoxazolyl, imidazolyl, and pyrazolyl; wherein R¹ is
25 phenyl optionally substituted at a substitutable position with one or more radicals selected from the group consisting of methyl, ethyl, isopropyl, butyl, tert-butyl, isobutyl, pentyl, hexyl, trifluoromethyl, cyano, carboxyl, methoxycarbonyl, hydroxyl,
30 hydroxymethyl, trifluoromethoxy, amino, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, nitro, methoxymethyl, methylsulfinyl, fluoro, chloro, bromo, methoxy, ethoxy, propoxy, n-butoxy, pentoxy, and methylthio; wherein R²
35 is amino; and wherein R³ is a radical selected from the group consisting of oxo, cyano, carboxyl, methoxycarbonyl, ethoxycarbonyl, carboxypropyl, carboxymethyl, carboxyethyl, cyanomethyl, fluoro,

chloro, bromo, methyl, ethyl, isopropyl, butyl, tert-butyl, isobutyl, pentyl, hexyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, fluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, methoxy, ethoxy, propoxy, n-butoxy, pentoxy, cyclohexyl, phenyl, pyridyl, thienyl, thiazolyl, oxazolyl, furyl, pyrazinyl, hydroxymethyl, hydroxylpropyl, benzyl, formyl, phenylcarbonyl, methoxymethyl, furylmethoxy, aminocarbonyl, N-methylaminocarbonyl, N,N-dimethylaminocarbonyl, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, aminomethyl, N,N-dimethylaminomethyl, N-methyl-N-ethylaminomethyl, benzyloxy, and phenyloxy; or a pharmaceutically-acceptable salt thereof.

9. The combination of Claim 8 wherein the cyclooxygenase-2 inhibitor is selected from compounds, their prodrugs and their pharmaceutically-acceptable salts, of the group consisting of

3-(3,4-difluorophenyl)-4-(4-methylsulfonylphenyl)-2-(5H)-furanone;
3-phenyl-4-(4-methylsulfonylphenyl)-2-(5H)-furanone;
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
4-[5-(3-fluoro-4-methoxyphenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
3-[1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-1H-imidazol-2-yl]pyridine;
2-methyl-5-[1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-1H-imidazol-2-yl]pyridine;
4-[2-(5-methylpyridin-3-yl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide;
4-[5-methyl-3-phenylisoxazol-4-yl]benzenesulfonamide;

4-[5-hydroxyethyl-3-phenylisoxazol-4-yl]benzenesulfonamide;

[2-trifluoromethyl-5-(3,4-difluorophenyl)-4-oxazolyl]benzenesulfonamide;

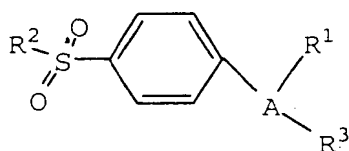
5 4-[2-methyl-4-phenyl-5-oxazolyl]benzenesulfonamide; and

4-[5-(3-fluoro-4-methoxyphenyl-2-trifluoromethyl)-4-oxazolyl]benzenesulfonamide.

10 10. The composition of Claim 1 wherein the leukocyte activation inhibitor is a cyclosporin.

11. The composition of Claim 10 wherein the cyclosporin is cyclosporin A.

15 12. A pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a therapeutically-effective amount of a leukotriene B₄ receptor antagonist, a cyclosporin and a cyclooxygenase-2 inhibitor selected from Dupont Dup 697, Taisho NS-398,
20 meloxicam, flosulide or compounds of Formula I



I

wherein:

25 A is a 5- or 6-member ring substituent selected from partially unsaturated or unsaturated heterocyclo or carbocyclic rings;

R¹ is at least one substituent selected from the group consisting of heterocyclo, cycloalkyl, cycloalkenyl and aryl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals selected from the group consisting of alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino,
30 nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and
35 alkylthio;

R² is selected from the group consisting of alkyl, and amino; and

R³ is a radical selected from the group consisting of halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocyclooxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclo, cycloalkenyl, aralkyl, heterocycloalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-arylaminalkyl, N-aralkylaminalkyl, N-alkyl-N-aralkylaminalkyl, N-alkyl-N-arylaminalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-arylaminosulfonyl, arylsulfonyl, and N-alkyl-N-arylaminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

13. The combination of Claim 12 wherein the cyclooxygenase-2 inhibitor is selected from compounds of Formula I.